

AMENDMENTS TO THE SPECIFICATION:

*Please replace the existing cross-reference to related applications section with the following replacement section.*

D<sup>1</sup>  
This application is also a continuation of U.S. Application No. 09/322,289, filed May 28, 1999, which is a continuation in part of U.S. Application No. 09/201,430, filed November 30, 1998, which claims the benefit under 35 U.S.C. § 119(e) of U.S. Application No. 60/080,970, filed April 7, 1998, and U.S. Application 60/067,740, filed December 2, 1997.

*Please replace the paragraph beginning on page 5, line 20 of the specification with the following replacement paragraphs.*

Figs. 15A-E: A $\beta$  levels in the cortex of 12-month old PDAPP mice treated with AN1792 or AN1528 in combination with different adjuvants. The A $\beta$  level for individual mice in each treatment group, and the median, mean, and p values for each treatment group are shown.

Fig. 15A: The values for mice for the PBS-treated control group and the untreated control group.

D<sup>2</sup>  
Fig. 15B: The values for mice in the AN1528/alum and AN1528/MPL-treatment groups.

Fig. 15C: The values for mice in the AN1528/QS21 and AN1792/Freund's adjuvant treatment groups.

Fig. 15D: The values for mice in the AN1792/Thimerosal and AN1792/alum treatment groups.

Fig. 15E: The values for mice in the AN1792/MPL and AN1792/QS21 treatment groups.

*Please replace the paragraph beginning at page 65, line 18, with the following replacement paragraph:*

D<sup>3</sup> To prepare vaccine doses with alum (Groups 1 and 5), A $\beta$  peptide in PBS was added to Alhydrogel (two percent aqueous aluminum hydroxide gel, Sargeant, Inc., Clifton, NJ) to reach concentrations of 100  $\mu$ g A $\beta$  peptide per 1 mg of alum. 10X PBS was added to a final dose volume of 200  $\mu$ l in 1X PBS. The suspension was then gently mixed for approximately 4 hr at RT prior to injection.

*Please replace the paragraph beginning at page 69, line 1, with the following replacement paragraph:*

D<sup>4</sup> The results of AN1792 or AN1592 treatment with various adjuvants, or thimerosal on cortical amyloid burden in 12-month old mice determined by ELISA are shown in Figs. 15A-15E. In PBS control PDAPP mice (Fig. 15A), the median level of total A $\beta$  in the cortex at 12 months was 1,817 ng/g. Notably reduced levels of A $\beta$  were observed in mice treated with AN1792 plus CFA/IFA (Fig 15C), AN1792 plus alum (Fig 15D), AN1792 plus MPL (Fig 15E) and QS21 plus AN1792 (Fig 15E). The reduction reached statistical significance ( $p < 0.05$ ) only for AN1792 plus CFA/IFA (Fig 15C). However, as shown in Examples I and III, the effects of immunization in reducing A $\beta$  levels become substantially greater in 15 month and 18 month old mice. Thus, it is expected that at least the AN1792 plus alum, AN1792 plus MPL and AN1792 plus QS21 compositions will achieve statistical significance in treatment of older mice. By contrast, the AN1792 plus the preservative thimerosal (Fig 15D) showed a median level of A $\beta$  about the same as that in the PBS treated mice. Similar results were obtained when cortical levels of A $\beta$ 42 were compared. The median level of A $\beta$ 42 in PBS controls was 1624 ng/g. Notably reduced median levels of 403, 1149, 620 and 714 were observed in the mice treated with AN1792 plus CFA/IFA, AN1792 plus alum, AN1792 plus MPL and AN1792 plus QS21 respectively, with the reduction achieving statistical significance ( $p = 0.05$ ) for the AN1792

D<sup>4</sup> CFA/IFA treatment group. The median level in the AN1792 thimerosal treated mice was 1619 ng/g A $\beta$ 42.

---

*Please replace the paragraph beginning at page 77, line 1, with the following replacement paragraph:*

---

D<sup>5</sup> To prepare vaccine doses with Freund's Adjuvant (Group 4), 100  $\mu$ g of AN1792 in 200  $\mu$ l PBS was emulsified 1:1 (vol:vol) with Complete Freund's Adjuvant (CFA) in a final volume of 400  $\mu$ l for the first immunization. For subsequent immunizations, the antigen was similarly emulsified with Incomplete Freund's Adjuvant (IFA). For the vaccines containing the adjuvants alum, MPL or QS-21, 100  $\mu$ g per dose of AN1792 or AN1528 was combined with alum (1 mg per dose) or MPL (50  $\mu$ g per dose) or QS-21 (25  $\mu$ g per dose) in a final volume of 200  $\mu$ l PBS and delivered by subcutaneous inoculation on the back between the shoulder blades. For the group receiving FA, 100  $\mu$ g of AN1792 was emulsified 1:1 (vol:vol) with Complete Freund's adjuvant (CFA) in a final volume of 400  $\mu$ l and delivered intraperitoneally for the first immunization, followed by a boost of the same amount of immunogen in Incomplete Freund's adjuvant (IFA) for the subsequent five doses. For the group receiving AN1792 without adjuvant, 10  $\mu$ g AN1792 was combined with 5  $\mu$ g thimerosal in a final volume of 50  $\mu$ l PBS and delivered subcutaneously. The ninth, control group received only 200  $\mu$ l PBS delivered subcutaneously. Immunizations were given on a biweekly schedule for the first three doses, then on a monthly schedule thereafter on days 0, 16, 28, 56, 85 and 112. Animals were bled six to seven days following each immunization starting after the second dose for the measurement of antibody titers. Animals were euthanized approximately one week after the final dose. Outcomes were measured by ELISA assay of A $\beta$  and APP levels in brain and by immunohistochemical evaluation of the presence of amyloid plaques in brain sections. In addition, A $\beta$ -specific antibody titers, and A $\beta$ -dependent proliferative and cytokine responses were determined.

---